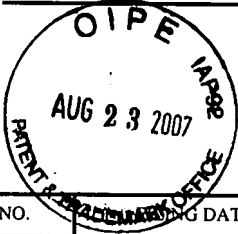




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APPLICATION NO.	FILED DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,057	10/24/2003	Joost A. Kolkman	022013-000170US	1548
7590 Joost A. Kolkman 2584 Cowper Street Palo Alto, CA 94301		08/09/2007		
			EXAMINER	
			LIU, SUE XU	
			ART UNIT	PAPER NUMBER
			1639	
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			08/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/693,057

Applicant(s)

KOLKMAN ET AL.

Examiner

Sue Liu

Art Unit

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 May 2007.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25-41 is/are pending in the application.
- 4a) Of the above claim(s) 34-41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 4/9/07; 5/17/07.

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claim Status

1. Claims 1-24 have been cancelled as filed 4/17/06.
Claims 25-41 are currently pending.
Claims 34-41 have been withdrawn.
Claims 25-33 are being examined in this application.

Election/Restrictions

2. Applicant's election with traverse of Group I invention (Claims 25-33) in the Reply filed on 8/15/06 is as previously acknowledged.
3. This application contains claims 34-41 drawn to an invention nonelected with traverse in the reply filed on 8/15/06. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
4. Applicants elected the following species:
 - A. A single species of a target molecule. Applicants elect "IgE".
 - B. A single species of a first monomer domain. Applicants elect an "LDL receptor class A monomer domain".
 - C. A single species of a second monomer domain. Applicants elect an "LDL receptor class A monomer domain".
 - D. A single species of a third monomer domain. Applicants elect an "LDL receptor class A monomer domain".in the Reply filed on 8/15/06 is as previously acknowledged.

Priority

5. This application is a CIP of 10/289,660 (filed on 11/06/2002; now ABN), which is a CIP of 10/133,128 (filed 04/26/2002), which claims benefit of the following provisional applications:

60/374,107 04/18/2002;

60/333,359 11/26/2001;

60/337,209 11/19/2001;

60/286,823 04/26/2001.

6. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention, which is also disclosed, in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/286,823, filed on 4/26/01, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. For examples, the '823 provisional patent does not provide support for LDL-receptor Class A domain and domains having 30-100 amino acids. The current application obtains the priority date of 60/337,209.

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Thus, the effective filing date of the instant application is 11/19/01.

Information Disclosure Statement

7. The information disclosure statements filed on 5/17/07 and 4/9/07 have been considered.
See the attached PTO 1449 form.

Oath/Declaration

8. The newly submitted ADS (5/17/07) to include the Inventor, Per-Ola Freskgard's information is acknowledged.

Claim Rejections Maintained

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

10. Claims 25-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

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art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

11. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue that the instant specification has demonstrated actual reduction to practice of the claimed invention. (Reply, p.7+). Applicants also argue that the present invention are not drawn to polypeptides of library of compositions, but methods for identifying a multimer that binds to a target molecule. (Reply, p.8).

Although the instant claims are reciting a method of identifying multimers, the recited method requires the reagents of "a library of polypeptides", "target molecules", "multimers", "monomer domains", etc. Without possession of the said reagents, the instant claimed methods cannot be accomplished. The instant method encompasses both screening for a "monomer domain", and using the identified monomer domain to make multimers that binds to a target.

The instant specification defines the term "monomer domain" or "monomer" broadly to encompass any "discrete region found in a protein or polypeptide" (p. 21 of the spec.). The monomer domains "forms a three-dimensional structure in solution", and can specifically bind to a target molecule (p. 21 of the spec.). The monomer domain can be of any size (p. 32, [133] of the spec.). The instant claim 25 recites "the monomer domains have 30-100 amino acids" (emphasis added), which can be broadly interpreted to mean that each of the monomer domains

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can have any number of amino acid residues that is above 30. Thus, any segment of polypeptide or protein with ≥ 30 amino acid residues that can bind to a target molecule is a "monomer" or a "monomer domain" as defined by the instant specification.

Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genus of monomers, and the genus of multimers that comprise of any combination of any "monomers". In addition, no representative numbers of species for each claimed genus is provided to show possession of the claimed genres of monomers and/or multimers.

The only examples of monomers and/or multimers are the LDL receptor A domain, and specific multimers formed with the LDL A domains (Examples 2-5, and 7-12), and one example of C2 domains (Example 6). Two examples of two types of monomer domains that can be manipulated and formulated into multimer proteins do not constitute a representative number of species of "monomers" and/or "multimers" for the claimed genres of monomers and/or multimers.

Although the instant specification briefly lists certain known domains in the art as examples of monomers, there is no specific discussion how these domains share common structure/functions. In addition, it has not been demonstrated by the instant disclosure that these protein domains (the purported "monomers") can be linked to other monomers, and to generate multimers that can bind the same target as one of the monomer unit in the multimer.

The state of prior art does not provide teachings of generating any multimers (any protein) from any monomers (e.g. any protein fragments). The state of art, however, does teach that the stability of proteins, especially heterologous proteins (proteins such as the ones of the

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instant claims), are highly unpredictable and may not be expressed (or made) properly. For example, Roodveldt et al (Current Opinion in Structural Biology. Vol. 15: 50-56; 2005), teach the problems that exist for generating heterologous proteins (e.g. non-natural proteins) such as production of insoluble proteins, and proteins that may be inactive or aggregated (p. 50, left and top of right cols). The Roodveldt reference also teaches that "it is largely unknown, however, how the stability of a protein is encoded in its sequence and how individual amino acid changes contribute to stability". Thus, the stabilities of proteins with various amino acid sequences are highly unpredictable, and hence the success of generating such proteins is also unpredictable.

The recited method of producing multimers that are composed of monomers (i.e. any protein fragments) is essentially a trial and error process that would involve identifying monomers that can be stably generated, and multimers that can be stably generated using the monomers. Without identifying the required monomers that can be used to establish the library of multimers, and without the successful generation of stable multimer proteins, the claimed method of screening the monomers and using the monomer to generate multimers against target molecules cannot be accomplished.

In addition, the case laws have addressed the issues of written description for methods using compounds that are yet to be identified.

"An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules

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selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.".)"

MPEP 2163. (emphasis added).

In this case, the instant specification nor the claims provided representative numbers of species or common structure for the claimed genus of polypeptides that are made or used in the claimed methods. The instant specification at best only describes "a wish or plan for obtaining" a monomer or a multimer for using to bind a target. Similar to the Rochester case, the instant disclosure has not demonstrated possession of the entire claimed genus of "monomers" or "multimers" for use in binding to a target. Applicant's claimed scope represents only an invitation to experiment regarding possible polypeptide.

Therefore, applicants are not in possession of the genres of monomers and/or multimers that can be successfully generated and used to screening for binding of a target molecule. Applicant's claimed broad scope of methods of screening various polypeptides represents only an invitation to experiment regarding possible monomers and/or multimer that may or may not be generated.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Scope of Enablement Rejection

12. Claims 25-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for generating libraries of monomers and/or multimers based on LDL receptor A domains alone, and C2 domains alone, does not reasonably provide enablement for generating other proteins that comprise any other monomers and/or multimers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

13. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants generally argue the claimed method is enabled in its full scope. (Reply, pp. 9+). Applicants also state "the relevant analysis concerns libraries, and not the stability of proteins in general". (Reply, p. 10).

Contrary to applicant's assertion, the discussion regarding the general stability of proteins is relevant to the instant claimed invention. The instant claims recite methods of screening "monomer domain", and using the identified "monomer domain" to generate "multimer domains" that can bind to a target. As discussed above, the instant specification defines the term "monomer domains" as "forms a three-dimensional structure in solution", and can specifically bind to a target molecule (p. 21 of the spec). Thus, the identified "monomer" or the generated

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“multimer domains” have property of forming “three-dimensional structure in solution” (soluble structures), and binding to specific targets.

As discussed in the previous Office action, the state of art indicate high unpredictability of generating proteins that are soluble and form proper structure, especially heterologous proteins (proteins such as the ones of the instant claims). For example, Roodveldt et al (Current Opinion in Structural Biology. Vol. 15: 50-56; 2005), teach the problems exist for generating heterologous proteins (e.g. non-natural proteins) such as production of insoluble proteins, and proteins that may be inactive or aggregated (p. 50, left and top of right cols). The Roodveldt reference also teaches that “it is largely unknown, however, how the stability of a protein is encoded in its sequence and how individual amino acid changes contribute to stability”. Thus, the stabilities of proteins with various amino acid sequences are highly unpredictable, and hence the success of generating such proteins is also unpredictable.

Besides the problems with generating stable proteins for using in various methods such as screening, exogenous (e.g. non-natural) proteins production requires considerations in many different areas. For example, Greene (Methods in Molecular Biology. Vol. 267: 3-14; 2004) teaches many potential problems with producing exogenous proteins (Abstract of the reference). Greene teaches problems related in the following areas: “translational compatibility” (p. 4+), “protein folding compatibility” (p. 6+), “protein solubility compatibility” (p. 7+), “posttranslational modification” (p. 8+), etc. Thus, it is highly unpredictable whether a particular exogenous protein can or cannot be properly produced using the known expression systems.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Barbas

15. Claims 25, 27, 28, 30, 31, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Barbas et al (US 6,140,466; 10/31/2000). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

16. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the Barbas reference does "not teach screening the library of polypeptides for affinity to a target molecule, identifying at least a first polypeptide comprising a first monomer domain that specifically binds to a target molecule, linking the first monomer domain to a plurality of different monomer domains to form a library of different multimers, the multimers comprising the first monomer domain and one of the plurality of different monomer domains, and screening the library of multimers for the ability to bind to the target molecule."
(Reply, p.12, para2).

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Applicants have made the above allegation without providing any reason or rationale as to why the teaching of the Barbas reference does not anticipate the claimed inventions.

As discussed in the previous office, the teaching of the Barbas reference anticipates the claimed invention. The detailed discussion of the previous office action is incorporated herein in its entirety, and recited below:

Barbas et al, throughout the patent, teach identifying or generating zinc finger polypeptides (reads on polypeptides comprising monomers and multimers) that bind to specific target nucleotides (Abstract of the reference).

The instant specification defines the term "monomer domain" or "monomer" broadly to encompass any "discrete region found in a protein or polypeptide" that can specifically bind to a target molecule (p. 21 of the spec.), and the monomer domain can be of any size (p. 32, [133]). Thus, any segment of polypeptide or protein that can bind to a target molecule is a "monomer" or a "monomer domain" as defined by the instant specification.

The zinc finger containing proteins taught by Barbas et al have "discrete regions" such as the different zinc finger regions (Figure 8A of Barbas), which either the individual "Fingers" (1-3) or the combination of the "Fingers" is a monomer domain according to the definition of the instant disclosure. The instant specification also discloses "zinc finger" as an example of "monomer" or "monomer domain" (p. 2, [20] of the instant spec.). Thus, the zinc finger regions taught by Barbas et al reads on the monomer domains of 30-100 amino acids of **clm 25**. As indicated by Figure 8 of the Barbas reference, "finger 1" has about 30 amino acids, and the combination of fingers 2 and 3 has about 60 amino acids. Furthermore, the reference also teaches a linker fused two three-finger proteins and multi-finger proteins (Abstract and Example 13 at col. 15, lines 20+ of Barbas), which each of the individual fingers and/or the combination of fingers (such as a two finger domain of about 60 amino acids) read on a monomer domain that has 30-100 amino acids.

Barbas et al also teach generating libraries of zinc finger proteins (through molecular cloning) and screening the libraries of zinc finger protein against nucleic acid target through binding assays (See Examples 1-14, especially, Examples 3 and 13), which reads on the screening of the library of polypeptides for affinity to a target molecule of **clm 25**, and the polynucleotides encoding the polypeptides of **clm 30**.

The reference teaches the generation of phage display library of zinc finger proteins with the size of 5×10^7 PFU (col. 40, lines 30+), which reads on at least 100 different polypeptides of **clm 31**.

Barbas also teaches randomization of amino acid residues only in the "finger 3" region of the zinc finger protein (Example 3 of Barbas), and thus holding other regions in the protein constant. The reference also teaches multiple panning procedure comprising several rounds of nucleic acid target recognition and replication (cols. 40-41). These read on linking the first monomer domain to a plurality of different monomer domains, forming multimers, and screening multimers against the target molecule of **clm 25**.

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The reference teaches each of the zinc finger of the zinc finger protein contains two cysteine residues (col. 1, lines 43+). The reference also teaches polypeptides comprising multiple "fingers" such as 3-12 fingers (col. 50, lines 30+), and thus a combination of three fingers that constitute as a "monomer" having six cysteines, as recited in **clm 27**.

The reference also teaches improved affinity for binding the target nucleic acid sequence of the mutated zinc finger protein (multimers) (col. 48, lines 32+), which reads on the increased affinity of **clm 28**.

The reference also teaches linking the zinc finger protein (with different numbers of monomers) to other protein domains (such as Jun/Fos leucine zippers and/or additional zinc fingers), and screening against target nucleic acid binding (see Examples 12-14), which reads on the trimers screening of **clm 33**.

Applicants also argue that the reference does not teach "walked" libraries or methods of using the them to identify a multimer (or any molecule) that binds to a target molecule. (Reply, p.14, para2).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "walked multimer library") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Esser

17. Claims 25-30, 32 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Esser et al (Journal of Biological Chemistry. Vol. 263: 13282-13290; 1988). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

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Discussion and Answer to Argument

18. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants state "Esser, et al., do not teach screening the library of polypeptides for affinity to a target molecule, identifying at least a first polypeptide comprising a first monomer domain that specifically binds to a target molecule, linking the first monomer domain to a plurality of different monomer domains to form a library of different multimers, the multimers comprising the first monomer domain and one of the plurality of different monomer domains, and screening the library of multimers for the ability to bind to the target molecule." (Reply, p.12, para4).

Applicants have made the above allegation without providing any reason or rationale as to why the teaching of the Esser reference does not anticipate the claimed inventions.

As discussed in the previous office, the teaching of the Esser reference anticipates the claimed invention. The detailed discussion of the previous office action is incorporated herein in its entirety, and recited below:

Esser et al, throughout the publication, teach mutational analysis of the ligand binding domain (reading on LDL receptor class A monomer domains of **clm 32**) of the human LDL lipoprotein receptor (see Figure 1), which indicates that each of the cysteine rich repeats of the LDL receptor has around 40-70 amino acids. The LDL receptor repeats and/or combination of the repeats read on the monomers, and the multimers of **clm 25**, and the trimer of **clm 33**.

The reference also teaches that the LDL receptor binds to various ligands (such as ApoB-100 of LDL and ApoE) through the cysteine-rich repeat regions (corresponding to the LDL receptor class A monomer domains), which reads on the protein target molecule of **clm 25 and 29**.

The reference teaches that the LDL receptor A domains are identified, and different mutations are generated in different A domains (or monomers) that are encoded by polynucleotides (see Figure 1 and p. 13283, right col.), which reads on the linking of an

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identified monomer with a plurality of different monomers (the repeats with different mutations) to form multimers (such as trimers), and screening for target binding multimers of **clms 25 and 33**, as well as polynucleotides of **clm 30**.

The reference also teaches that mutations in different cysteine-rich sequences (the different monomer domains) lead to different binding specificity to different ligands (see Abstract, Tables I and II, and p. 13287+ of the reference), which reads on the increased binding specificity of **clm 28**.

It is known in the art that the six cysteine residues in each of the cysteine-rich repeats (monomer domains) inherently form disulfide bonds as evidenced by Fass et al (Nature: Vol. 388: 691-693; 1997), and therefore the structure taught by the reference (Esser et al) reads on the disulfide bond and six cysteines of **clms 26 and 27**.

Applicants also argue that the reference does not teach "walked" libraries or methods of using the them to identify a multimer (or any molecule) that binds to a target molecule. (Reply, p.14, para2).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "walked multimer library") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Bajari

19. Claims 25-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Bajari et al (Biological Chemistry. Vol. 379: 1053-1062; Aug/Sept., 1998). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

20. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants state "Bajari, et al., do not teach screening the library of polypeptides for affinity to a target molecule, identifying at least a first polypeptide comprising a first monomer domain that specifically binds to a target molecule, linking the first monomer domain to a plurality of different monomer domains to form a library of different multimers, the multimers comprising the first monomer domain and one of the plurality of different monomer domains, and screening the library of multimers for the ability to bind to the target molecule." (Reply, p.13, para 2).

Applicants have made the above allegation without providing any reason or rationale as to why the teaching of the Bajari reference does not anticipate the claimed inventions.

As discussed in the previous office, the teaching of the Bajari reference anticipates the claimed invention. The detailed discussion of the previous office action is incorporated herein in its entirety, and recited below:

Bajari et al, throughout the publication, teach using phage display to screen for LDL receptor A domain (LR8 fragments) or variants thereof that bind to a protein target (see Abstract).

The reference teaches the LR8 fragment of the LDL receptor is the LDL receptor type A domain (p. 379, right col.), which reads on LDL receptor class A monomer domains of **clm 32**. The reference also teaches the LR8 repeats have more than 30 amino acid residues, and have six cysteines (see Figures 1 and 2; p. 1055, left col.). The LR8 repeats and/or combination of the repeats read on the monomers, and the multimers of **clm 25**, the trimer of **clm 33**, and the six cysteines of **clm 27**.

The reference also teaches disulfide bridges (or bonds) formed by the six cysteine residues (p. 1058, right col., middle of para 1), which reads on the disulfide bonds of **clm 26**.

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The reference also teaches that the screening (or panning target) is receptor associated protein (RAP) (Abstract and p. 1059, left col., para 2), which reads on the protein target molecule of **clm 25 and 29**.

The reference teaches that the LDL receptor A domains are identified, and different mutations are generated in different A domains (monomers or repeats) that are encoded by polynucleotides (p. 1059, left col.), which reads on the linking of an identified monomer with a plurality of different monomers (the repeats with different random mutations) to form multimers (such as trimers), and screening for target binding multimers of **clms 25 and 33**, as well as polynucleotides of **clm 30**.

The reference also teaches that isolated LR8 domains have high affinity to the ligand (p.1057, right col., and pp. 1055-1056, bridging para), which reads on inherent property of increased binding specificity of the multimers of **clm 28**.

The reference teaches the library has 10^8 phages (containing different polypeptides), and isolation of 120 phage clones (p. 1055, left col.), which reads on the at least 100 different polypeptides of **clm 31**.

Applicants also argue that the reference does not teach "walked" libraries or methods of using the them to identify a multimer (or any molecule) that binds to a target molecule. (Reply, p.14, para2).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "walked multimer library") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Etzerodt

21. Claims 25-31 and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by Etzerodt et al (US 2004/0132094 A1; 7/8/2004; priority date: 2/28/2001). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

22. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants state "Etzerodt, et al., do not teach screening the library of polypeptides for affinity to a target molecule, identifying at least a first polypeptide comprising a first monomer domain that specifically binds to a target molecule, linking the first monomer domain to a plurality of different monomer domains to form a library of different multimers, the multimers comprising the first monomer domain and one of the plurality of different monomer domains, and screening the library of multimers for the ability to bind to the target molecule." (Reply, p.14, para 1).

Applicants have made the above allegation without providing any reason or rationale as to why the teaching of the Etzerodt reference does not anticipate the claimed inventions.

As discussed in the previous office, the teaching of the Etzerodt reference anticipates the claimed invention. The detailed discussion of the previous office action is incorporated herein in its entirety, and recited below:

Etzerodt et al, throughout the publication, teach libraries of proteins that comprise C-type Lectin-like domains, and the methods of generating such libraries (see Abstract of the reference).

The reference teaches the C-type lectin-like domains (CTLDs) has approximately 50 to 70 amino acid residues, as indicated by Table 1 and Figure 1 of the reference (p. 2-3 and [0007]), which the CTLDs read on the monomer domains of **clm 25** as defined by the instant specification (see the discussion above regarding the definition for "monomer").

The reference teaches generating libraries of proteins that comprise mutant CTLDs (p. 18, [0176]+) and screening the library against target molecules ([0188]), which reads on the screening of the library of polypeptides comprising different monomer domains of **clm 25**.

The reference teaches that the protein libraries are generated based on tetranectin CTLD and the tetranectin is trimeric in nature ([0046] and [0192]), and generation and screening of

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multimeric libraries ([0071])- [0076]; and Claims 1-29; especially Claims 10 and 13), which read on the screening of multimers and trimers of **clms 25 and 33**.

The reference teaches the CTLDs contain six cysteine residues (see Figure 1), and contain two or three intra-chain disulfide bridges (or bonds) ([0004]), which read the disulfide bond of **clm 26** and the six cysteines of **clm 27**.

The reference teaches screening the combinatorial libraries (monomer or multimer libraries) based on affinity selection, and "isolating progressively better binder by repeated rounds of panning and re-amplification (Claim 29 of the reference), which read on the increased affinity of **clm 28**.

The reference teaches the CTLDs (such as tetranectin) bind to various targets including plasminogen, fibrinogen/fibrin, and apolipoprotein, which reads on the target is a protein of **clm 29**.

The reference teaches the libraries of polypeptides are encoded by polynucleotides (Claim 22 of the reference), which reads on the polynucleotides of **clm 30**.

The reference teaches the sizes (such as 10^{11}) of the phage display libraries used to express the libraries of polypeptides ([0225]), which reads on at least 100 different polypeptides of **clm 31**.

Applicants also argue that the reference does not teach "walked" libraries or methods of using the them to identify a multimer (or any molecule) that binds to a target molecule. (Reply, p.14, para2).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "walked multimer library") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Esser and Bajari

24. Claims 25-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Esser et al (Journal of Biological Chemistry. Vol. 263: 13282-13290; 1988), in view of Bajari et al (Biological Chemistry. Vol. 379: 1053-1062; Aug/Sept., 1998). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

25. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue that "the Examiner has failed to provide references teaching the elements of the invention and has not articulated any reasoning or rationale to arrive at the claimed invention or to support the Examiner's conclusion of obviousness." (Reply, p.15, para 3).

Applicants have made the above allegation without providing any reason or rationale as to why the teaching of the combination of references does not render obvious the claimed

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inventions. The detailed discussion of the previous office action is incorporated herein in its entirety, and recited below:

Esser et al, throughout the publication, teach mutational analysis of the ligand binding domains (reading on LDL receptor class A monomer domains) of the human LDL lipoprotein receptor, as discussed above.

Esser et al do not specifically teach the at least 100 different polypeptides comprising the monomers and/or multimers, as recited in **clm 31**.

However, Bajari et al, throughout the publication, teach using phage display to screen for LDL receptor A domains (LR8 fragments) or variants thereof that bind to a protein target, as discussed above. The reference also teaches the display library contains at least 100 different polypeptides, as discussed above. In addition, the reference teaches the advantages of screening large libraries such as the approach would allow developments of diagnostics and/or therapeutics of interest (Abstract of the Bajari reference). The reference further teaches the screening of phage libraries (containing a large number of polypeptides) would allow isolation of high affinity polypeptides that are in soluble form (p. 1057, last para).

Thus, a person of ordinary skill in the art would have been motivated at the time of the invention to screen large libraries of polypeptides (at least 100 polypeptides) to isolate the desired polypeptides with high target binding affinity, due to the fact that Bajari teaches the advantages and the need to screen large libraries to isolate polypeptides of interest. A large library contains more diverse polypeptides as taught by Bajari (10^8 phages; p. 1055, left col.), and thus would allow higher probability of success of isolating a desired target.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since Bajari et al have demonstrated the success of screening libraries of monomers (LDL receptor A domains) containing at least 100 different polypeptides.

Applicants also argue that the reference does not teach "walked" libraries or methods of using the them to identify a multimer (or any molecule) that binds to a target molecule. (Reply, p.14, para2).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "walked multimer library") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Double Patenting

26. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

'256

27. Claim 25-33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11, 15-17, and 20-26 of copending Application No. 11/281,256 (20060234299; filed 11/16/05). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

28. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in *italic*):

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Applicants argue the provisional ODP rejection should be withdrawn because no other rejections are remaining. (reply, p.16, para 7).

However, the instant claims are remain rejected, and thus the above ODP rejection is maintained for the reason of record.

'245

29. Claim 25-33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 11/281,245 (20060223114; filed 11/06/2005). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

30. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the provisional ODP rejection should be withdrawn because no other rejections are remaining. (reply, p.16, para 7).

However, the instant claims are remain rejected, and thus the above ODP rejection is maintained for the reason of record.

'064

31. Claim 25 and 33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 207-214 of copending Application No.

10/966,064 (20050221384; filed 10/15/04). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

32. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the provisional ODP rejection should be withdrawn because no other rejections are remaining. (reply, p.16, para 7).

However, the instant claims are remain rejected, and thus the above ODP rejection is maintained for the reason of record.

'679

33. Claim 25-33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-32 of copending Application No. 10/971,679 (20050164301; filed 10/22/04). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

34. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

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Applicants argue the provisional ODP rejection should be withdrawn because no other rejections are remaining. (reply, p.16, para 7).

However, the instant claims are remain rejected, and thus the above ODP rejection is maintained for the reason of record.

'602

35. Claim 25-33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 5-11, 21, 29, 33, 36, 78, and 98 of copending Application No. 10/871,602 (20050089932; filed 6/17/04). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

36. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the provisional ODP rejection should be withdrawn because no other rejections are remaining. (reply, p.16, para 7).

However, the instant claims are remain rejected, and thus the above ODP rejection is maintained for the reason of record.

'723

37. Claim 25-33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 5-11, 13, 16, 23, 29, 33, 36, 78, and 98

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of copending Application No. 10/840,723 (20050053973; filed 5/5/2004). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

38. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the provisional ODP rejection should be withdrawn because no other rejections are remaining. (reply, p.16, para 7).

However, the instant claims are remain rejected, and thus the above ODP rejection is maintained for the reason of record.

'351

39. Claim 25, 26, and 28-33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18, 21-24, 29-31 and 34-36 of copending Application No. 10/957,351 (20060008844; filed 1/12/2006). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

40. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

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Applicants argue the provisional ODP rejection should be withdrawn because no other rejections are remaining. (reply, p.16, para 7).

However, the instant claims are remain rejected, and thus the above ODP rejection is maintained for the reason of record.

'989

41. Claim 25-33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 15, 18-21, and 24-27 of copending Application No. 11/155,989 (20060177831; filed 6/17/05). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Discussion and Answer to Argument

42. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the provisional ODP rejection should be withdrawn because no other rejections are remaining. (reply, p.16, para 7).

However, the instant claims are remain rejected, and thus the above ODP rejection is maintained for the reason of record.

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Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SL
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7/24/07

**/Jon D. Epperson/
Primary Examiner, AU 1639**



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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)		<i>Complete if Known</i>			
		Application Number	10/693,057		
		Filing Date	October 24, 2003		
		First Named Inventor	Kolkman, et al.		
		Art Unit	1639		
		Examiner Name	LIU, Sue Xu		
Sheet	1	of	8	Attorney Docket No: 022013-000170US	

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
/SL/		US-6140466	10-31-2000	BARBAS, III; Carlos F. et al.	
		US-2004132094A1	07-08-2004		
		US-20050053973	03-10-2005	KOLKMAN; Joost A. et al.	
		US-20050089932	04-28-2005	KOLKMAN; Joost et al.	
		US-20050221384	10-06-2005	KOLKMAN; Joost A. et al.	
		US-20060008844A1	01-12-2006	STEMMER; Willem P. C. et al.	
		US-20060177831	08-10-2006	STEMMER; Willem P. C. et al.	
		US-2006223114A1	10-05-2006	STEMMER; Willem P. C. et al.	
		US-2006234299A1	10-19-2006	STEMMER; Willem P. C. et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³ - Number ⁴ -Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		EP-623679A1	11-09-1994	Micromet Ag		<input type="checkbox"/>
		EP-640130	04-15-1998	Creative Biomolecules, Inc.		<input type="checkbox"/>
		WO-0034784	06-15-2000	Phylos, inc.		<input type="checkbox"/>
		WO-0060070	10-12-2000	Innogenetics N.V.		<input type="checkbox"/>
		WO-0075308	12-14-2000	Skerra, Arne		<input type="checkbox"/>
		WO-0127147	04-19-2001	The University of Queensland et al.		<input type="checkbox"/>
		WO-0157065	08-09-2001	Diversys Limited		<input type="checkbox"/>

EXAMINER SIGNATURE

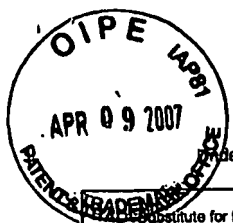
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07/24/2007

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		Examiner Name	LIU, Sue Xu		
Sheet	2	of	8	Attorney Docket No: 022013-000170US	

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ - Number ⁴ -Kind Code ⁵ (if known)				
/SL/		WO-0177342	10-18-2001	Genentech, Inc.		<input type="checkbox"/>
		WO-0204523	01-17-2002	Research Corporation Technologies, Inc. et al.		<input type="checkbox"/>
		WO-0212277	02-14-2002	Diversys Limited		<input type="checkbox"/>
		WO-0232925	04-25-2002	Phylos, Inc. et al.		<input type="checkbox"/>
		WO-9106305	05-16-1991	Bristol-Myers Squibb Company		<input type="checkbox"/>
		WO-9111461	08-08-1991	Biogen, Inc. et al.		<input type="checkbox"/>
		WO-9117173	11-14-1991	Cytogen Corporation		<input type="checkbox"/>
		WO-9323537	11-25-1993	Creative Biomolecules et al.		<input type="checkbox"/>
		WO-9411403	05-26-1994	Mosbach, Klaus et al.		<input type="checkbox"/>
		WO-9428173	12-08-1994	Affymax Technologies N.V. et al.		<input type="checkbox"/>
		WO-9519567	07-20-1995	The Trustees of Columbia University in the City of New York et al.		<input type="checkbox"/>
		WO-9637621	11-28-1996	Morphosys Gesellschaft fuer Proteinoptimierung MbH et al.		<input type="checkbox"/>
		WO-9721829	06-19-1997	Merck Patent GmbH		<input type="checkbox"/>
		WO-9856906	12-17-1998	Larsen, Ingrid, Kjeller		<input type="checkbox"/>
		WO-9856915	12-17-1998	Research Corporation Technologies, Inc.		<input type="checkbox"/>
		WO-9916873	04-08-1999	Skerra, Arne		<input type="checkbox"/>
		WO-9919276	04-22-1999	ALNIS, LLC et al.		<input type="checkbox"/>
		WO-9945110	09-10-1999	Diatech Pty. Ltd.		<input type="checkbox"/>

NON PATENT LITERATURE DOCUMENTS

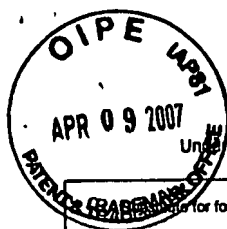
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/Sue Liu/

DATE CONSIDERED 07/24/2007

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Sheet	3	of	8	Attorney Docket No: 022013-000170US	

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T2
/SL/		ADAMS G. et al., Generating improved single-chain Fv molecules for tumor targeting, J. of Immunol Methods, 1999, 231 (1-2), 249-260.	
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		ARNDT K. et al., A heterodimeric coiled-coil peptide pair selected in vivo from a designed library-versus-library ensemble, J. Mol Biol., 2000, 295 (3), 627-639.	
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		BESTE G. et al., Small antibody-like proteins with prescribed ligand specificities derived from the lipocalin fold, PNAS(USA), 1999, 96 (5), 1898-1903.	
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		Filing Date	October 24, 2003		
		First Named Inventor	Kolkman, et al.		
		Art Unit	1639		
		Examiner Name	LIU, Sue Xu		
Sheet	4	of	8	Attorney Docket No: 022013-000170US	

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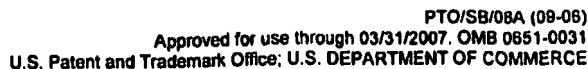
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Art Unit	1639
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Examiner Name	LIU, Sue Xu
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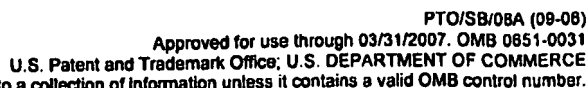
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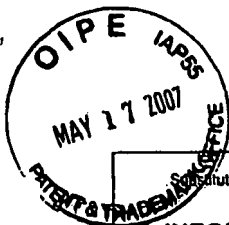
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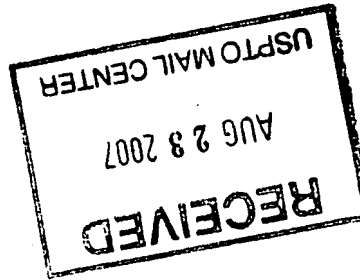
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